مورنینگ روز شنبه ۲۴ شهریور ماه

# نحوه اپروچ به نفروپاتی دیابتی در خانم ۵۵ ساله در درمانگاه پزشکی خانواده

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CC

خانم ۵۵ ساله مراجعه با دیابت

# PI

خانم ۵۵ ساله مورد دیابت نوع ۲ که از ۱۰ سال قبل تشخیص و درمان شروع شده است.
جهت پیگیری روتین بیماری و ارائه جواب ازمایشات مراجعه کرده است که در ازمایش ادرار البومینوری مشهود است.
از سه سال قبل جهت بیمار انسولین تراپی اغاز شده است اما به علت عدم همکاری کامل بیمار در تزریق انسولین و همچنین عدم رعایت سبک زندگی مناسب همچنان قند های بیمار کنترل نمیباشد.
بیمار شکایت از پرنوشی و پرادراری مختصر دارد.
شرح حال از کاهش حجم ادرار نمیدهد. شرح حالی از دیزوری یا بوی بد ادرار یا هماچوری و درد پهلو و تب نمیدهد.

# History

PMH: دیابت نوع دو از ۱۰ سال قبل.

DH: انسولین لانتوس ۲۵ واحد روزانه
انسولین نوورپید ۸ واحد قبل از هر وعده غذایی

AH: منفی
HH: منفی
FH: دیابت نوع دو در مادر و خواهر و برادر

# Phy E

V.S: PR:76 BP:158/94 RR:16 SPO2:99%
T:36.6

خانم ۵۵ ساله هشیار و اورینته. Ill و toxic نمیباشد.
اسکلرا pale و ایکتریک نیست.
سمع قلب و ریه نرمال است.
شکم نرم و بدون ارگانومگالی و بدون تندرنس میباشد.
CVA Tenderness: ندارد
اندام ها: بدون ادم و تورم میباشد.

# Lab

CBC
Wbc:8000
Hb:13.5
Plt:217000

Cr: 1.5
GFR:41
(CKD EPI)

FBS: 186
HbA1c: 8.7

U/A
Pr+++
Glu+
Wbc-
Rbc-
Bact-
Alb: 955
mg/d
ACR:31.8
mg/g

# Problem list

خانم ۵۵ ساله مورد دیابت نوع دو poor control تحت درمان با انسولین که در ازمایشات رایز کراتینین و البومینوری مشهود است.

# Objectives

- What are the stages of diabetic nephropathy.
- Diagnosis of diabetic nephropathy.
- Approach of prevention of diabetic nephropathy.
- New and updated management of diabetic nephropathy.

**Diabetic nephropathy is a clinical syndrome characterized by the following :**

- Persistent albuminuria (>300 mg/d) with or without a raised serum creatinine level, that is confirmed on at least 2 occasions 3-6 months apart.
- **Progressive decline in the glomerular filtration rate (GFR).**
- Elevated arterial blood pressure.

# Risk factors

Several factors may increase the risk of diabetic nephropathy, including:

- **High blood sugar** that's difficult to control (sustained hyperglycemia HBA1c > 8.6).
- **High blood pressure** (hypertension) that's difficult to control.
- **High blood cholesterol.**
- Being a smoker.
- A family history of diabetes and kidney disease.
- Retinopathy.

# 1 – Stages of Diabetic Nephropathy

Diabetes

Diagnosis

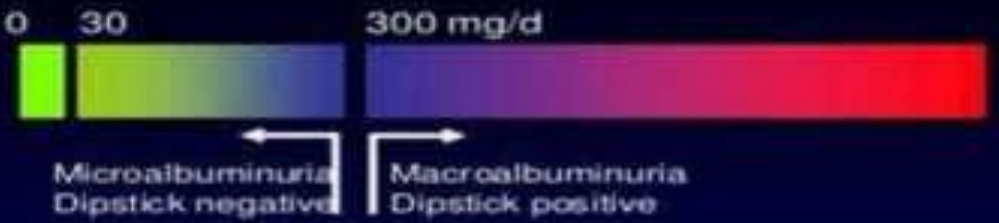
Hyperfiltration

Clinical Latency

Microalbuminuria

Macroalbuminuria

Renal failure




New Terminology

Micro-albuminuria = High Albuminuria

Macroabuminurai = Very high Albuminuria

# DN: Stages

| | |
|---|---|
| Stage 1 | • Glomerular hypertension and hyperfiltration<br>• Normoalbuminuria: urinary albumin excretion rate (AER)<br>• Raised GFR, normal serum creatinine |
| Stage 2 | • "Silent phase" (structural changes on biopsy but no clinical manifestations)<br>• Normoalbuminuria |
| Stage 3 | • Microalbuminuria: AER<br>• Normal serum creatinine<br>• There may be increased blood pressure |
| Stage 4 | • Overt "dipstick positive" proteinuria (macroalbuminuria) : AER<br>• Hypertension<br>• Serum creatinine may be normal<br>• Increase in serum creatinine with progression of nephropathy |
| Stage 5 | • End stage renal failure<br>• Requiring dialysis or transplant to maintain life |

# 2 – Diagnosis of Diabetic Nephropathy

# Screening

A test for the presence of microalbuminuria should be performed:

- At diagnosis in patients with type 2 diabetes and
- After 5 years of diagnosis with type 1 diabetes

Screening for microalbuminuria can be performed by

Measurement of the albumin-to-creatinine ratio in a random spot collection.

Albumin: Creatinine Ratio (ACR) should be measured using a morning urine sample, however random urine samples can be used

Measurement of urinary albumin can be influenced by a number of factors including:

- Urinary tract infection
- High dietary protein intake
- Vaginal discharge or menstruation
- Drugs (NSAIDS)
- Congestive heart failure
- Acute febrile illness
- Uncontrolled BS
- Uncontrolled BP
- Extreme exercise

# Microalbuminuria

- **American guideline:** 2.5 – 25 mg/mmol in male and 3.5 – 35 mg/mmol in female.
- **Australian guideline:** 2.5 – 25 mg/mmol in male and 3.5 – 35 mg/mmol in female.
- **British guideline:** (NICE) 2.5 – 30 mg/mmol in male and 3.5 – 30 mg/mmol in female.
- **Canadian guideline**: 2 – 20 mg/mmol in both male and female.

To confirm microalbuminuria:

- Perform additional ACR measurements 1 to 2 times within 3 months.
- Microalbuminuria is confirmed if at least 2 of 3 tests (including the screening test) are positive.

# How to calculate GFR

- There is some website provide eGFR calculation.

  Ex: http://egfrcalc.renal.org/
- Also there are some equation.

❑ Ex: **the MDRD equation**

**GFR** (mL/min/1.73 $m^2$) = 175 × $(S_{cr})^{-1.154}$ × $(Age)^{-0.203}$ × (0.742 if female) × (1.212 if African American)

http://nephron.org/mdrd_gfr_si

❑ Ex: **the Cockcroft-Gault formula**

**GFR** (mL/min/1.73 $m^2$) = (140 – Age) × Weight in Kg × (1.04 if female – 1.23 if malr) / serum creatinine in mmol/L

http://touchcalc.com/calculators/cg

# Indications for renal biopsy

1. Severely elevated albuminuria
2. RBC casts, dysmorphic RBCs , or WBC casts
3. Presence of another systemic disease
4. A sudden increase albuminuria or a rapid decline in eGFR

# 3- Prevention of Diabetic Nephropathy

# Prevention of Diabetic Nephropathy

- Patient education is the key in trying to prevent DN.
- Appropriate education, follow-up, and regular doctor visits are important in prevention of DN.

- Glycemic control reduces the onset of microalbuminuria and slow progression of DN.

  **Evidence Level I**

- Control of blood preasure in diabetic patients reduce progression of DN.

  **Evidence Level I**

- ACEi and ARBs decrease progression of kidney dysfunction.

  **Evidence Level I**

- Smoking increases risk of development and progression of CKD in people with type 2 diabetes.

  **Evidence Level II**

# 4- Management of Diabetic Nephropathy

Normotensive persons with diabetes and microalbuminuria should be given an ACE inhibitor or ARB to reduce progression to macroalbuminuria

Persons with type 1 or 2 DM and microalbuminuria should continue to be tested for albuminuria **annually** to monitor disease progression and response to therapy

| Drug Name (Trade Name) | Starting Dose | Goal Dose* |
|---|---|---|
| ***ACE Inhibitors*** | | |
| Benazepril (Lotensin) | 10 mg daily | 20-40 mg/d in 1-2 divided doses |
| Captopril (Capoten) | 6.25-25 mg 3 times per day | 25-150 mg 2 or 3 times per day |
| Enalapril (Vasotec) | 5 mg daily | 10-40 mg daily in 1-2 divided doses |
| Fosinopril (Monopril) | 10 mg daily | 20-80 mg daily |
| Lisinopril (Prinivil, Zestril) | 10 mg daily | 20-40 mg daily |
| Moexipril (Univasc) | 7.5 mg daily | 7.5-30 mg daily in 1-2 divided doses |
| Perindopril (Aceon) | 4 mg daily | 4-16 mg daily in 1-2 divided doses |
| Quinapril (Accupril) | 10-20 mg daily | 20-80 mg daily in 1-2 divided doses |
| Ramipril (Altace) | 1.25 mg daily (CCr <40 mL/min/1.73 $m^2$)<br>2.5 mg daily | 1.25-20 mg daily in 1-2 divided doses |
| Trandolopril (Mavik) | 1 mg daily | 2-4 mg daily |
| ***ARBs*** | | |
| Candesartan (Atacand) | 16 mg as monotherapy | 2-32 mg daily in 1-2 divided doses |
| Eprosartan (Teveten) | 600 mg daily (monotherapy) | 400-800 mg daily in 1-2 divided doses |
| Irbesartan (Avapro) | 150 mg daily | 150-300 mg daily |
| Losartan (Cozaar) | 25-50 mg daily | 25-100 mg daily in 1-2 divided doses |
| Olmesartan (Benicar) | 20 mg daily (monotherapy) | 20-40 mg daily |
| Telmisartan (Micardis) | 40 mg daily | 40-80 mg daily |
| Valsartan (Diovan) | 80 or 160 mg daily | 80-320 mg daily |

*Goal doses should be at the higher end of the dose range when possible

Combination therapy with ACE inhibitors and angiotensin II receptor blockers should be avoided in persons with diabetes, atherosclerosis, and evidence of end-organ damage

- In type 1 diabetes the evidence for the superiority of ACE is clear, ARB used if ACE is contraindicated or can't be tolerated.
- In type 2 diabetes the evidence for the superiority of ACE inhibitors is less clear.
- Some evidence went to superiority of ARB.

- Treat people with type 1 diabetes and microalbuminuria with an ACE inhibitor irrespective of blood pressure. An ARB may be used if an individual is intolerant of an ACE inhibitor.
- Treat people with type 2 diabetes and microalbuminuria with an ACE inhibitor or an ARB irrespective of blood pressure.

Scottish Intercollegiate Guidelines Network

When should patient with diabetic nephropathy referred to nephrologists:

- Once microalbuminuria is diagnosed.
- Once macroalbuminuria is diagnosed.
- If there is rapid progression of chronic kidney disease.
- Stage 3 chronic kidney disease (estimated glomerular filtration rate 30 – 59 mL per minute per 1.73 $m^2$).

# Referral to nephrologists

- Acute kidney injury
- Rapid progression of chronic kidney disease
- Stage 4 chronic kidney disease (estimated glomerular filtration rate < 30 mL per minute per 1.73 $m^2$)

American Diabetic Association (diabetic care)

# Home messages

- Screening of microalbuminuria at diagnosis in type 2 DM and after 5 years of diagnosis with type 1 DM.
- Microalbuminuria is confirmed with positive 2 of 3 tests.
- Patient education is the cornerstone in preventing DN.
- Patient with DN should be offered ACE or ARB even if normotensive.
- Patients with microalbuminuria should be tested for albuminuria **annually** to monitor disease progression and response to therapy.

# case

خانم ۵۵ ساله مورد دیابت نوع دو poor control تحت درمان با انسولین که در ازمایشات رایز کراتینین و البومینوری مشهود است.

# Management

- سونوگرافی
- توصیه به رعایت رژیم غذایی
- ورزش
- بررسی از نظر رتینوپاتی
- کنترل چربی با توجه به لیپید پروفایل
- کنترل فشار خون با دارویی مانند والزارتان
- کنترل قند خون با تنظیم انسولین و اضافه کردن دارویی از دسته های glp1 (liraglutide/semaglutide) و یا sglt2 (empagliflozin)

# سطوح پیشگیری

**Primordial Prevention**

**Primary Prevention**

**Secondary Prevention**

**Tertiary Prevention**

**Quaternary Prevention**

# Primordial Prevention

- آموزش پزشکان و مراقبین سلامت در این زمینه
- توصیه های تغذیه در سطح کلان مثل صداوسیما
- تشکیل پرونده الکترونیک سلامت برای تمام بیماران مبتلا به دیابت

# Primary Prevention

- توصیه های life style به بیماران مبتلا به دیابت

# Secondary Prevention

- بررسی ازمایشات تشخیص زودهنگام نفروپاتی دیابتی
- کنترل قند خون و فشار خون برای کاهش پیشرفت نفروپاتی دیابتی

# Tertiary Prevention

- درمان نفروپاتی با ACE inhibitors یا ARBs

# Quaternary Prevention

- عدم درمان همزمان با ACE inhibitors & ARBs